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| 09/155,003 | 09/14/1998 | LUIS ENJUANES SANCHEZ | ACY-33261 | 7916 |

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| EXAMINER | |
|---|---|
| PARKIN, JEFFREY S | |
| ART UNIT | PAPER NUMBER |
| 1648 | 8 |

DATE MAILED: 01/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/155,003 | Sanchez, L. E., et al. |
| **Examiner** | **Art Unit** |
| Jeffrey S. Parkin, Ph.D. | 1648 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *12 Oct 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *46-64* is/are pending in the application.

4a) Of the above, claim(s) *46-56 and 60-64* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *57-59* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## Detailed Office Action

### *Status of the Claims*

1. Applicants' election with traverse of Group VI (claims 57-59) in paper no. 5 is acknowledged. The traversal is based upon the premise that the same corresponding technical feature is present in each invention. This argument is not deemed to be persuasive for the reasons of record previously set forth in paper no. 4. Applicants are reminded that the claimed invention fails to make a contribution over the prior art (i.e., see the ISA Chapter I search report and Chapter II preliminary examination report). Moreover, the claims are clearly directed toward multiple products with different components. These groups were clearly identified in the original restriction requirement as follows:

a. Group I, claims 46-48, drawn to a recombinant **expression vector** comprising a **defective viral genome** encoding a selected **antigen**.

b. Group II, claims 46, 47, and 49, drawn to a recombinant **expression vector** comprising a **defective viral genome** encoding a selected **antibody**.

c. Group III, claims 50-52, 55, and 56, drawn to a recombinant expression system comprising an **expression vector** encoding a selected **antigen** and **helper virus**.

d. Group IV, claims 50, 53, 54, 55, and 56, drawn to a recombinant expression system comprising an **expression vector** encoding a selected **antibody** and **helper virus**.

e. Group V, claims 57 and 64, drawn to a vaccine comprising an **expression vector** encoding a selected **antibody**, a **helper virus**, and **pharmaceutically acceptable excipient**.

f. Group VI, claims 57-59, drawn to **porcine vaccine** comprising an expression vector encoding a porcine pathogenic immunogen, a helper virus, and a pharmaceutically acceptable excipient.

g. Group VII, claims 57, 60, and 61, drawn to a **canine vaccine** comprising an expression vector encoding a canine pathogenic immunogen, a helper virus, and a pharmaceutically acceptable excipient.

h. Group VIII, claims 57, 61, and 62, drawn to a **feline vaccine** comprising an expression vector encoding a feline pathogenic immunogen, a helper virus, and a pharmaceutically acceptable excipient.

Contrary to applicants' assertions, each of the inventions in these groups have different compositions and will require separate searches. Furthermore, many of the groups bear no structural similarities (i.e., an antigen is structurally different and unrelated to an antibody) so a special technical feature could not possibly be present. Therefore, the **requirement is still deemed to be proper and is therefore made FINAL.** Claims 46-56 and 60-64 are withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

***Disclosure***

2. The disclosure is objected to because of the following informalities: page 4 references SEC DI No. 24 which should read SEQ ID NO.: 24 or something similar thereto. Appropriate correction is required.

***35 U.S.C. § 112, Second Paragraph***

3. Claims 57-59 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite for referencing characteristics of a non-elected invention. Applicants are reminded of the restriction requirement set forth in paper no. 4. The claims should be amended to reflect this election (i.e., A vaccine ... comprising a nucleic acid encoding an antigen/immunogen ...).

The reference to an "infectious agent having tropism for mucoses" is also confusing since the precise target tissue is vague and indefinite. It is suggested that applicants amend the claim

language to indicate that the pathogen of interest displays a tropism for mucosal surfaces, mucosal tissues, mucosal linings, or something similar thereto.

The reference to a vaccine comprising a "recombinant expression system" which comprises an expression vector, helper virus, and pharmaceutical excipient is confusing since the precise components of the vaccine are not readily manifest. Moreover, the claim language fails to clearly set forth the salient characteristics of the claimed invention. For instance, does the vaccine composition actually consist of a DNA vaccine comprising two different nucleotide sequences encoding an immunogen and a helper virus or does the vaccine comprise a single nucleotide sequence encoding an immunogen admixed with a helper virus? Alternatively, are the claims directed toward a recombinant virus produced by transfecting cells infected with a helper virus with an expression vector comprising a TGEV DI-based expression vector? Applicants should clearly and unambiguously set forth the components of the vaccine composition. Moreover, it is not readily manifest what is encompassed by the term "expression system". Does this reference a single nucleotide sequence comprising a recombinant expression vector capable of encoding a heterologous antigen? Does this reference a subgenomic single nucleotide sequence encoding an antigen (i.e., a DNA vaccine)? Does this sequence reference a defective interfering particle that is capable of encoding a foreign antigen? Appropriate correction and clarification are required.

The reference to a helper virus is also confusing since it is not readily manifest what function the helper virus provides. The vaccine already contains a "recombinant expression system" which presumably leads to the production of significant quantities of the immunogen of interest. However, it is not readily manifest which complementary viral proteins and functions are provided by the

helper virus. A helper virus generally provides some sort of packaging function that is missing from the defective parent construct. Appropriate correction and clarification are required.

***35 U.S.C. § 112, First Paragraph***

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 57-59 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are broadly directed toward vaccines comprising "recombinant expression systems" encoding antigens derived from infectious agents that have a tropism for "mucoses". The disclosure describes the preparation of an expression vector comprising genomic segments derived from a transmissible gastroenteritis (TGEV) coronavirus defective interfering (DI) particles which were designated DI-A or DI-C. Heterologous inserts placed within these constructs are regulated by the TGEV gene S promoter. Cells were transfected with these constructs and helper virus (THER-1) provided to facilitate the packaging of viruses comprising the antigens of interest. Appropriately drafted claim language directed toward these embodiments would be acceptable (i.e., A vaccine composition comprising a recombinant virus carrying a heterologous antigen and TGEV DI particle genome ...).

The legal considerations that govern enablement determinations

pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the preparation of suitable expression vectors. As noted *supra*, the disclosure describes the preparation of recombinant expression vectors carrying TGEV DI particle genomes. However, the disclosure fails to describe the preparation of any other suitable expression vectors or systems.

2) It has been well-documented in the prior art that many DI particles are not suitable expression vectors because of expression, packaging, and stability problems (see also the disclosure, p. 2). The disclosure fails to provide adequate guidance pertaining to those portions of the genome, particularly as it applies to TGEV, that are required for the construction of a suitable expression vector. Moreover, many mucosally directed vaccine strategies fail to induce systemic immunity (Mestecky *et al.*, 1994). Thus, the selection of an expression vector and suitable antigen are critical. However, the disclosure is silent concerning these issues.

3) The disclosure only provides a two working embodiment involving TGEV DI-C- and DI-A-based constructs. The disclosure fails to provide any guidance pertaining to other suitable constructs.

4) The claims are of excessive breadth and fail to receive adequate support from the disclosure. The first paragraph of § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C. 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). The court in *In re Vaeck* reported that while "It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art. *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." The disclosure fails to provide sufficient guidance that would lead the skilled artisan to other species.

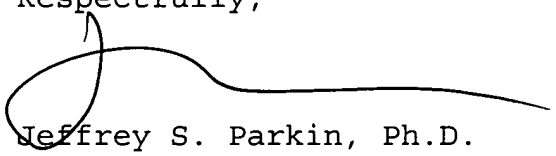
Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

***Correspondence***

6. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

7. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,



Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

28 December, 2001